

REMARKS

Claims 1-25 are pending in the instant application. The examiner has maintained the rejection of claims 1-25 under 35 USC §103(a) in view of a combination of references. First, the examiner has rejected claims 1-17 over Goertz (US, 4,801,460) and Ortega (US 4,837,032). Second, the examiner maintains that claims 17-25 of the instant invention are unpatentable over Noda (US 5,389,380) in view of Goertz. For the reasons below, applicants respectfully request the rejection be withdrawn and the application be passed to issue.

1. Response to rejection under 35 USC §103 in view of Goertz and Ortega

The examiner argues that one of ordinary skill in the art would have been motivated to prepare the instant composition in light of Goertz which discloses "a process of preparing sustained release theophylline composition where the process comprises heating a mixture of N-vinylpyrrolidone and vinyl acetate and theophylline at a temperature of 120° (examples 1 and 3)." Paper number 7, p. 7, 2nd paragraph. However, applicants' respectfully assert that Goertz does not teach a process comprising heating a mixture of N-vinylpyrrolidone and vinylacetate.

Goertz teaches a process of melt-extrusion of either a fusible NVP polymer (col. 1 line 55 to col 2, line 17) which is either a homopolymer obtained from N-vinylpyrrolidone as a monomer or a copolymer obtained by copolymerization of the monomers N-vinylpyrrolidone and vinylacetate. (Column 5, lines 3-10). The resulting copolymer forms a new polymer with essentially different properties from a mixture of

two homopolymers. Goertz further discloses that the copolymer is admixed with an active ingredient, and the mixture is then processed by melt-extrusion, wherein the copolymer must be molten. (Column 2, lines 25-30).

Specifically, Goertz discloses:

The polymeric binder must soften or melt in the total mixture of all components at from 50 to 180°C., preferably from 60°C to 130°C., so that the melt can be extruded.

Column 2, lines 25-28.

In contrast, the instant invention utilizes polyvinylpyrrolidone grades with a molecular weight of 20,000 to 1,000,000. Utilization of polyvinylpyrrolidone at these molecular weights results in compositions with higher glass transition temperatures. Thus, the process of the instant invention, carried out at a maximum temperature of 130°C does not produce melt in the granulation. (Page 5, lines 10-15 of applicant's specification). For instance, polyvinylpyrrolidone with a molecular weight of 40,000 melts at 168°C. Support for this may be found in the attached affidavit of Dr. Karl submitted in applicants amendment on May 27, 2003. In the affidavit Kolter describes the glass transition temperature of polyvinylpyrrolidone as a function of molecular weight. The data supplied therein clearly shows that as the molecular weight of polyvinylpyrrolidone increases, the glass transition temperature also increases.

The examiner argues that Goertz is silent as to molecular weight and that polyvinyl pyrrolidone of any molecular weight can be used with the range of heating

temperature. However, one of ordinary skill in the art would interpret Goertz as inherently teaching the molecular weight of the polymers as Goertz specifically requires the melting of the polymer. That is, Goertz explicitly requires melting of the polymer which is dependent on the glass transition which is a function of the molecular weight. Accordingly, because Goertz requires melting [it] one of ordinary skill in the art would understand that it necessarily limits the molecular weight of the polyvinyl pyrrolidone.

Furthermore, the modification to the Goertz reference would render the invention unsatisfactory for its intended purposed. Under MPEP 2143.01, a suggestion or motivation to make the proposed modification does not exist if the proposed modification would render the prior art invention unsatisfactory for its intended purpose. MPEP §2143.1 *citing In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). As quoted above, Goertz requires that the polymer binder must soften or melt so that the melt can be extruded. Absent this melt, it is not possible for the melt to be extruded. Accordingly, the examiner's suggestion that Goertz may be carried out with any molecular weight would render the invention unsatisfactory for its intended purpose, to be extruded. Therefore, the Goertz reference cannot support a suggestion or motivation to combine the references.

The process of the instant invention, carried out at a maximum temperature of 130°C does not produce melt in the granulation. For instance, polyvinylpyrrolidone with a molecular weight of 40,000 melts at 168°C. It is clear from this evidence that the polyvinylpyrrolidone does not melt during the granulation step of the instant process as

polyvinylpyrrolidone of the molecular weights of claim 1 show a glass transition temperature above 130°C. Accordingly, the instant invention comprises a mixture of polyvinylpyrrolidone and vinyl acetate in contrast to the polymer as disclosed in Goertz.

Furthermore, the examiner argues that the instant invention is obvious in view of Ortega. However, Ortega discloses sustained release tablets formulated by wet granulating a mixture of theophylline and the acid insoluble polymer. (Column 4, lines 4-10). The instant process does not require the addition of a solvent or binder solution. Thus, Ortega discloses a very different process than that of the instant invention. Under MPEP 2143.01, if a proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. MPEP 2143.01, *citing In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). Accordingly the Ortega reference, requiring wet granulation, is not sufficient to render the instant invention *prima facie* obvious.

Together, the Goertz and Ortega references do not render the instant invention obvious. As discussed above the Goertz reference requires melting of the N-vinylpyrrolidone polymer in order to be extruded and Ortega requires a solvent suitable for a wet granulation process. Together, these references do not teach each and every element of the claimed invention. Namely, the references do not teach polyvinylpyrrolidone of a molecular between 20,000 to 1,000,000 wherein the formulated mixture of polyvinylacetate and polyvinylpyrrolidone acts both as binder and

a matrix former.

Thus, the instant invention is not a combination of known compositions as the examiner suggests. The instant invention is different from the Goertz and Ortega in that the claimed process does not contain a completely molten mixture nor does it use wet granulation. As Goertz and Ortega operate by different principles it is improper to use these references to support a *prima facie* case of obviousness. Moreover, modifying Goertz in the manner suggested would render the invention unsatisfactory for its intended use. Accordingly, these references do not suggest to one of ordinary skill in the art the mixture of the present invention. Therefore, the combination of the references fails to establish a *prima facie* case of obviousness.

2. Response to rejection under 35 USC §103 in view of Noda and Goertz

The examiner argues that claims 17-25 are obvious in view of 35 USC §103(a) in view of Goertz and Noda (US 5,389,380). Noda discloses a sustained release pharmaceutical preparation comprising a carrier, an effective ingredient layer and a coating layer. Thus, Noda teaches that a coating layer is necessary to achieve sustained release of the active ingredient. (Column 3, lines 35-40). Moreover, the coating layer requires a heat-meltable material as a binder. (Column 3, lines 50-55).

In contrast to the disclosure of Noda, the instant invention does not require melt in the granulation. Moreover, a *prima facie* case of obviousness has not been identified as, in the very least, there is no suggestion that it is possible to combine the active

ingredient in the coating layer. Thus, one of ordinary skill in the art would not have a reasonable expectation of success in combining a mixture of polyvinylpyrrolidone with the active ingredient, without melt, where the prior art teaches a covering layer to control the release of the pharmaceutical ingredient and requires polymeric melt.

Under MPEP 2143.01, if a proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. MPEP 2143.01, citing *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). As discussed above, Noda teaches a process where cores coated with layers are produced however, the instantly claimed process produces granules having a matrix structure and not particles with a core with coating layers.

Accordingly, the combination of Goertz and Noda does not render the instant invention obvious as both of the references would lead one to believe that a heat meltable material is required to provide sustained release of the pharmaceutical preparation. As discussed above, the modification suggested by the examiner would render Goertz inoperable for its intended purpose. Second, Noda discloses a different principle of operation and under the MPEP it is not proper to utilize this type of reference to establish a *prima facie* case of obviousness. Moreover, neither reference suggests that it is possible to utilize a non-meltable material to achieve the desired result. Accordingly, these references in combination cannot be combined to render the instant invention obvious. Thus, applicant's respectfully request the rejection be

withdrawn as the references fail to establish a *prima facie* case of obviousness.

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Respectfully submitted,

KEIL & WEINKAUF

A handwritten signature in black ink, appearing to read 'Lesley E. Shaw', with a stylized flourish at the end.

Lesley E. Shaw
Reg. No. 52,214

LES/lc

1350 Connecticut Ave., N.W.
Washington, D.C. 20036
(202)659-0100

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